

Dr P Mikesell

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Pasteur's "attenuation"
has baffled me for 35 years or
more; and I was fascinated
to see your account in ASM
News.

Would you favor me with
your papers on this subject?

Do your experiments show
that heat cures with respect
to the plasmid (compare kappa in
Paramecium) vs. selects for
plasmid-free variants?

Sincerely
Joshua Lederberg

Dulles

THE ROCKEFELLER UNIVERSITY, NEW YORK, N.Y.

Plasmids, Pasteur, and Anthrax

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Few microbial pathogens have had as great an impact on the development of the science of medical bacteriology as *Bacillus anthracis*. This organism is the etiological agent of anthrax (Greek: "coal, carbuncle, pustule"), a historical disease of considerable economic importance. Anthrax-like infections are described in ancient literature, including the biblical Book of Exodus, which describes the disease as the fifth plague of Egypt. Anthrax epizootics were responsible for enormous domestic livestock losses in Europe from the seventeenth through the nineteenth century. The first infections in animals in the United States were documented in the Louisiana Territory in the early eighteenth century. The disease spread throughout the South and Northeast, and in the 1820s the first human cases of anthrax in this country were reported in Kentucky. Since the early 1900s, there has

been a gradual decline in the incidence of anthrax in humans in the United States. This is attributed to three major factors: (i) the use of a vaccine for individuals deemed at risk, (ii) better working conditions for those exposed to wool, hides, and animal products, and (iii) less exposure to imported contaminated animal products (2).

History of Anthrax Research

Although anthrax dates back more than 2,000 years, it was not recognized as a disease until the eighteenth century. Maret in 1752 and Fournier in 1769 both described the "malignant pustule" in humans, and Chabert in 1780 described the disease in animals (19). However, no connection between the two diseases was made for the next 80 years. In 1853, Barthelémy demonstrated transmission of the disease by inoculating blood from infected animals

into healthy animals (18), and 15 years later the anthrax bacillus was observed microscopically by Delafond (2). During the 1850s and 1860s, numerous studies established that (i) blood from anthrax-infected animals contained large, nonmotile bacilli, (ii) inoculation of healthy animals with blood or tissue containing these bacilli engendered the disease, and (iii) the "malignant pustule" in humans contained bacilli similar to those found in animals with anthrax. Yet it was not until 1877 that Robert Koch conclusively proved that there was a causal relationship between the large nonmotile bacilli and the disease of anthrax (18). In so doing Koch became the first to demonstrate that a specific bacterium was responsible for a specific disease. This work resulted in the formulation of Koch's ~~postulates~~ postulates, which established the framework of theory and practice for the development of the science of medical microbiology.

In France in the late 1870s anthrax was a severe disease that destroyed flocks of sheep throughout the French countryside. This destruction influenced Louis Pasteur to direct his attention to the study of anthrax. Pasteur had just developed a regimen for heat attenuation of

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